694

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THE INFLUENCE OF ANDROGEN ON BLADDER FUNCTION AND BLOOD VESSEL THE EXAMINATION INCLUDING HISTOLOGICAL CHANGE OF BLADDER AND VESSEL IN USING SHR RAT

Hypothesis / aims of study

There are only occasional reports on relation between androgen and bladder function. On the other hand, we occasionally saw the reports for a relation between blood vessel and androgen1). In addition, it is reported that vascular risk factors in relation to arteriosclerosis indicate they play a important role to generate LUTS and OAB 2). SHR rat has hypertension that is one of the vascular risk factors. Also, it is reported that the influence of hypertension gives to a bladder function 3). So we examined the relativity of androgen and bladder function from the aspect of bladder blood flow. In this study, we examined the effect of androgen on bladder blood flow, effect on the reaction to bladder irritability and histological change after androgen deprivation using castrate SHR rat model.

Study design, materials and methods

1. The difference of blood flow by the affection of sex hormone

We used over 8 week-old mature male SHR rat. We utilized following groups to our experiment (n=8 rats for each group); 12 -weeks after castration group (Group C), SHR rat control group for Group C (Group S), Wistar rat control group(Group W). Blood flow of the bladder was measured by Fluorescent microsphere method. Left carotid artery of the rats were cannulated and a constant quantity of fluorescent microspheres were injected intra-arterially, then bladder was excised and weighted. Blood Flow rate is shown as absorbance rate of bladder weight per 1g×reference blood retrieval rate(ml/min)/absorbance rate of entire microsphere within the reference blood（ml/min/g）.

2. Androgen and bladder function, examination of reaction to irritative symptoms

Bladder cystostomy was created under pentobarbital sodium anesthesia using polyethylene tube and one week later, cystometry was performed without anesthesia or restraint. Bladder was irrigated with Saline(NS), then 0.25% acetic acid(AA) liquid solution for 1hour with the speed of 5ml/h. As to micturition parameter, we defined as follows, maximum voiding pressure, voiding interval and single voided volume.

3. Examination of histological change of Bladder and Blood Vessel by Sex hormone

All rats were sacrificed, bladders and vessels of from abdominal aorta to iliac artery were removed. Examine the difference of mucosa, smooth muscle and quantity of collagen fiber. One pathologist classified it in 1+ , 2+ or 3+ depending on degree of the histological change.

Results

1. The difference of bladder blood flow by sex hormone

By fluorescent microsphere method, the bladder blood flow of each group were 1.37±0.30, 1.44±0.47, 1.45±0.48(mL/min/g), respectively for C, S and W group. No difference of bladder blood flow was shown according to deprivation of sex hormone(Fig1).

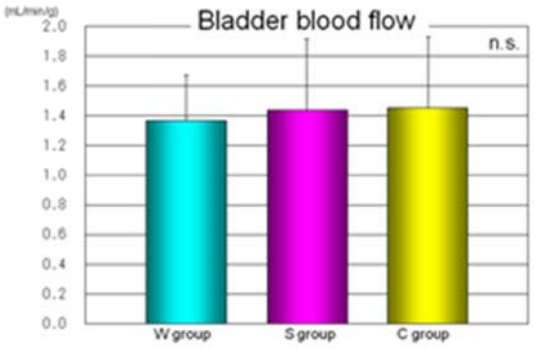

Fig1: The difference of bladder blood flow by sex hormone

2. Androgen and bladder function, examination of reaction to irritative symptoms

Maximum voiding pressure, there was no significant difference in the maximum voiding pressure between the NS irrigation and AA irrigation among Group C, Group S and Group W (34.39±4.41 to 38.97±2.41 , 33.38±5.36 to 34.60±5.75 , 35.67±3.65 to 37.04±2.84(cmH2O), respectively for 3 groups).

Voiding Interval, in Group C, Group S and Group W (564.84±172.02 to 288.50±114.34, 403.50±140.57 to 291.14±160.74 , 482.67±69.17 to 201.35±78.43(sec)), among all groups AA group was shortened significantly. ($p<0.01$) . And at the examination of NS group, C group compare to S group was extended significantly. ($p<0.01$) (Fig2).

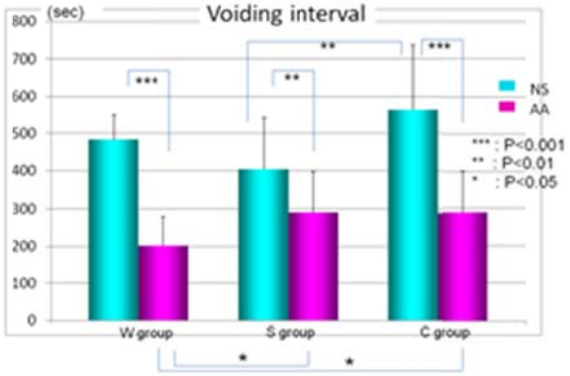

Fig2: Androgen and bladder function, Voiding Interval
Single Voided Volume,

Single Voided Volume, in Group C, Group S and Group W(0.696±0.29 to 0.522±0.084 , 0.358±0.15 to 0.334±0.17 , 0.467±0.15 、0.441±0.21(mL)), among all groups in AA group was decreased but significant difference was not shown. At the examination of AA group, C group compare to S group was increased significantly ($p<0.05$).

3. Examination of histological difference of bladder and blood vessel by sex hormone
In the histological examination, fibrosis at bladder was shown in C group compared to W group significantly ($p<0.01$). The examination of the iliac artery was similar results.
The examination of the abdominal aorta, fibrosis was shown in C group and S group compared to W group significantly ($p<0.01$) (Fig3).

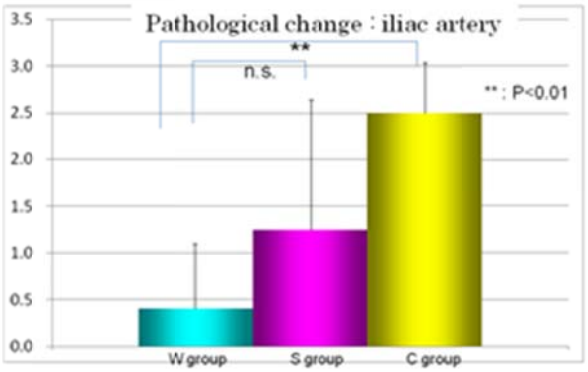

Fig3: Pathological change by sex hormone; iliac artery

Interpretation of results
Bladder blood flow does not show the change with androgen deprivation at the time of reviewing SHR rat and it is considered the blood flow involvement will be less for bladder function. Fibrosis is seen in bladder and artery by androgen deprivation histologically and we considered it could be possible for histological change to influence on bladder function. In addition, a part of relation between androgen and blood vessel could be confirmed as well.

Concluding message
This is the first report for considering androgen deprivation and bladder function by using SHR rat. Furthermore, the report for confirming the histological change of common iliac artery with androgen deprivation was also provided for the first time. We consider the results at this time would be important results that clarify a relation between androgen and blood vessel, bladder function.

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Ethical approval
We carried out all animal experiment under approval of Gunma University animal experiment committee.

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Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**We carried out all animal experiment under approval of Gunma University animal experiment committee.**